

The statistical properties of protein folding in the ϕ^4 theory

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Abstract

The statistical properties of protein folding within the ϕ^4 model are investigated. The calculation is performed using statistical mechanics and path integral method. In particular, the evolution of heat capacity in term of temperature is given for various levels of the nonlinearity of source and the strength of interaction between protein backbone and nonlinear source. It is found that the nonlinear source contributes constructively to the specific heat especially at higher temperature when it is weakly interacting with the protein backbone. This indicates increasing energy absorption as the intensity of nonlinear sources are getting greater. The simulation of protein folding dynamics within the model is also refined.

Keywords: protein folding, model, nonlinear

1. Introduction

It is well known that the time ordered of protein folding is realized from the primary to the secondary and subsequent structures. Furthermore, the secondary structure consists of the shape representing each segment of a

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polypeptide tied by hydrogen bonds, van der Walls forces, electrostatic interaction and hydrophobic effects. It is also formed around a group of amino acids considered as the ground state, and extended to include adjacent amino acids till the blocking amino acids are reached and the whole protein chain along the polypeptide adopted its preferred secondary structure. However, such mechanism has not yet been understood at the satisfactory level. For instance, the studies based on statistical analysis of identifying the probabilities of locating amino acids in each secondary structure are still at the level of less than 75% accuracy. Moreover, the main mechanism responsible for a structured folding pathway have also not yet been identified at all. Although, it is believed that such protein misfolding has been identified as the main cause of several diseases like cancers and so on [1].

On the other hand, some previous studies have shown that the nonlinear excitations could play an important role in conformational dynamics of protein backbone by decreasing the effective binding rigidity of a biopolymer chain leading to a buckling instability of the chain [2]. The results motivate us to develop a model describing the conformational changes of protein based on the ϕ^4 theory [3]. The model is actually inspired by some previous models which attempt to reproduce the protein folding using nonlinear Schrödinger hamiltonian with the additional tension-like force [4, 5]. Those explain the transition of a protein from a metastable to its ground conformation induced by solitons, while the mediator of protein transition is the Davydov solitons propagating through the protein backbone [6]. It has been shown that our model could reproduce and improve such models more naturally from first principle using lagrangian formalism. Another known theoretical study for the conformational dynamics of biomolecules is the so-called ab initio quantum chemistry approach which, however requires astronomical computational power to deal with realistic biological systems [7, 8]. In contrary, along with the current model there are also some attempts to describe the dynamics in term of elementary biomatter using field theory approach [9] and open quantum system [10, 11].

This paper follows the same model in [3] to describe the protein folding dynamics. In contrast with the previous works adopting nonlinear Schrödinger equation and putting the required interactions by hand, e.g. [4, 6, 5], the ϕ^4 term in the present model produces nonlinear Klein-Gordon equation as a source of disturbance, that is the ϕ^4 self-interaction generates the nonlinear and tension force terms naturally [11]. In the model, the protein backbone is assumed linear for the initial condition. Then the nonlinear bunch of the

light, like a laser, passed to the backbone. The interaction between the conformational changes and nonlinear source leads to certain U(1) symmetry breaking. This would be the main source of protein folding. However more than investigating its dynamics as done in such previous works [3, 5], this paper deals with statistical properties involved in the process. In particular, the focus is put on the heat capacity in a certain volume, C_V , representing the energy absorption against the temperature changes. The effect of nonlinear sources on C_V is investigated.

The paper is organized as follows. First, the model and the underlying assumptions are briefly reviewed in detail in Sec. 2. It is then followed by the short derivation of relevant equation of motions (EOMs) as done in [3] and showing the refined numerical simulation of folding process within the model. In Sec. 4 the statistical mechanics properties are investigated in detail. Finally the paper is concluded with summary and discussion.

2. The Models

Let us briefly review the model proposed in our previous work [3]. The lagrangian density in the model is given as,

$$l_{tot} = l_c(\phi) + l_s(\psi) + l_{int}(\phi, \psi), \quad (1)$$

where,

$$l_c = \frac{1}{2} \left[(\partial_\mu \phi)^\dagger (\partial^\mu \phi) + m_\phi^2 (\phi^\dagger \phi) \right], \quad (2)$$

$$l_s = \frac{1}{2} \left[(\partial_\mu \psi)^\dagger (\partial^\mu \psi) - \frac{1}{2} \lambda (\psi^\dagger \psi)^2 \right], \quad (3)$$

$$l_{int} = \Lambda (\phi^\dagger \phi) (\psi^\dagger \psi), \quad (4)$$

representing the conformational changes of a protein backbone and the nonlinear source injected to the backbone, while the last one is the interaction term between both.

From the lagrangian, the total potential working in the system can be written as,

$$V(\psi, \phi) = -\frac{\lambda}{4} (\psi^\dagger \psi)^2 + \Lambda (\phi^\dagger \phi) (\psi^\dagger \psi). \quad (5)$$

Imposing a local U(1) symmetry to the total lagrangian and considering its minima lead to the vacuum expectation value (VEV),

$$\langle\psi\rangle = \sqrt{\frac{2\Lambda}{\lambda}}\langle\phi\rangle. \quad (6)$$

This non-zero VEV then yields the so-called spontaneous symmetry breaking. On the other hand, substituting $\langle\psi\rangle$ into Eq. (5) induces the 'tension force' which plays an important role to enable folded pathways appear naturally.

The symmetry breaking at the same time shifts the ϕ mass as follow,

$$m_\phi^2 \rightarrow \bar{m}_\phi^2 \equiv m_\phi^2 - \frac{2\Lambda^2}{\lambda}\langle\phi\rangle^2. \quad (7)$$

Roughly, $\langle\phi\rangle$ and m_ϕ are at the same order. Then one can obtain a constraint for the couplings as follow,

$$1 - \frac{2\Lambda^2}{\lambda} > 0 \text{ or } 2\Lambda^2 < \lambda, \quad (8)$$

to guarantee the positive masses.

Now we are ready to move further on investigating the dynamics and statistical properties of protein folding within the model.

3. Dynamics of EOMs

Having the total lagrangian in Eq. (1) at hand, one can derive immediately respective EOMs using Euler-Lagrange equation in term of ψ and ϕ [3],

$$\left(\frac{\partial^2}{\partial x^2} - \frac{1}{c^2} \frac{\partial^2}{\partial t^2} - \frac{1}{\hbar^2} m_\phi^2 c^2 - 2\Lambda \psi^2 \right) \phi = 0, \quad (9)$$

$$\left(\frac{\partial^2}{\partial x^2} - \frac{1}{c^2} \frac{\partial^2}{\partial t^2} - 2\Lambda \phi^2 + \lambda \psi^2 \right) \psi = 0. \quad (10)$$

Note that from now the natural unit is restored to make the light velocity (c) and \hbar appear explicitly in the equations.

Since the EOMs under consideration are coupled nonlinear partial differential equations, then one should in principle solve them numerically. The numerical solution are done using the forward finite difference method [12].

Both coupled EOMs in Eqs. (9) and (10) are rewritten in explicit discrete forms as follows,

$$\begin{aligned} u_{i,j+1} &= 2u_{i,j} - u_{i,j-1} + c^2\epsilon^2 \left(\frac{u_{i+1,j} - 2u_{i,j} + u_{i-1,j}}{\delta^2} - 2\Lambda w_{i,j}^2 u_{i,j} + \lambda u_{i,j}^3 \right), \\ w_{i,j+1} &= 2w_{i,j} - w_{i,j-1} + c^2\epsilon^2 \left(\frac{w_{i+1,j} - 2w_{i,j} + w_{i-1,j}}{\delta^2} - 2\Lambda u_{i,j}^2 w_{i,j} \right. \\ &\quad \left. - \frac{c^2}{\hbar^2} m_{\phi_c}^2 w_{i,j} \right), \end{aligned} \quad (12)$$

for $i = 2, 3, \dots, N-1$ and $j = 2, 3, \dots, M-1$. In finite difference scheme, it is more convenient to replace ψ and ϕ with u and w respectively. The following boundary conditions for both fields must be deployed,

$$\begin{aligned} \psi(0, t) &= \psi(L, t) = 0 \quad \text{and} \quad \phi(0, t) = \phi(L, t) = 0 \quad \text{for } 0 \leq t \leq b, \\ \psi(x, 0) &= f(x) \quad \text{and} \quad \phi(x, 0) = p(x) \quad \text{for } 0 \leq x \leq L, \\ \frac{\partial \psi(x, 0)}{\partial t} &= g(x) \quad \text{and} \quad \frac{\partial \phi(x, 0)}{\partial t} = q(x) \quad \text{for } 0 < x < L, \end{aligned} \quad (13)$$

with $f(x)$, $p(x)$, $g(x)$ and $q(x)$ are newly introduced auxiliary functions. The discretized value between these boundary conditions consists of $(N-1) \times (M-1)$ rectangles with side length $\Delta x = \delta$ and $\Delta t = \epsilon$, where the side lengths must be very small to reduce truncation error.

In order to calculate Eqs. (11) and (12) across the whole region, two lowest initial values must be given. On the other hand, the value at t_1 is fixed by the boundary conditions in Eq. (13). The second order of Taylor expansion can also be used to determine the values in the second row. Therefore, the values at t_2 are determined by,

$$u_{i,2} = f_i - \epsilon g_i + \frac{c^2\epsilon^2}{2} \left(\frac{f_{i+1} - 2f_i + f_{i-1}}{\delta^2} - 2\Lambda p_i^2 f_i + \lambda f_i^3 \right), \quad (14)$$

$$w_{i,2} = p_i - \epsilon q_i + \frac{c^2\epsilon^2}{2} \left(\frac{p_{i+1} - 2p_i + p_{i-1}}{\delta^2} - 2\Lambda f_i^2 p_i - \frac{c^2}{\hbar^2} m_{\phi_c}^2 p_i \right), \quad (15)$$

for $i = 2, 3, \dots, N-1$. Initially, let us assume that the nonlinear source has a particular form of $f(x) = 2\operatorname{sech}(2x) e^{i2x}$ and $g(x) = 1$ to generate the α -helix, while $q(x) = 0$ for the sake of simplicity. Then, one can obtain the next lowest initial values in this case using Eqs. (14) and (15). The subsequent values are generated by substituting the preceding values into Eqs. (11) and (12). The higher order values can be obtained using iterative procedure.

In this paper, the simulation is done using the following values for the relevant parameters (in natural units) : $m = 0.08$ eV, $L = 2.364$ nm, $\Lambda = 0.0028$, $\lambda = 0.0003$. It should be emphasized that these values satisfy the constrain in Eq. (8). The result is given in Fig. 1. This result is also a revised version of the previous one reported in [3] which contains some technical errors, although the conclusion remains the same.

The left figure in each box describes the propagation of nonlinear sources in protein backbone, while the right one shows how the protein is folded. As can be seen in the figure, the protein backbone is initially linear before the nonlinear source injection. As the soliton started propagating over the backbone, the conformational changes appear. It should be remarked that the result is obtained up to the second order accuracy in Taylor expansion. In order to guarantee that the numerical solutions do not contain large amount of truncation errors, the step sizes δ and ϵ are kept small enough. Nevertheless, this should be good approximation to describe visually the mechanism of protein folding.

4. Statistical mechanics

Now let us discuss the main part of this paper. The statistical properties of a system with a particular lagrangian can be investigated through its partition function. It should be emphasized that the statistical observables hold only on an equilibrium which is fortunately guaranteed in the present case since the lagrangian under consideration is just the well known Klein-Gordon scalar lagrangian.

The statistical observables can be conveniently calculated from the generating functional by the perturbation method [13]. The generating functional for scalar fields is written as,

$$Z = \int \mathcal{D}\phi \mathcal{D}\psi \exp \left\{ i \int d^2x l_{tot}(\phi, \psi) \right\}. \quad (16)$$

The partition function can further be obtained from the generating functional by implementing a Wick rotation of the real axis [14], *i.e.* by defining the imaginary time $it = \tau$. Considering the finite time, the integral is performed between the range of $-\beta/2 \sim \beta/2$ with a periodicity condition of the field, that is $\phi(0, -\frac{\beta}{2}) = \phi(L, \beta/2)$. Here, L is a fixed boundary of one dimensional space of protein backbone, while $\beta = 1/T$ with T is the absolute temperature

in Kelvin. This specifically leads to the finite temperature case in Euclidean coordinates,

$$Z = \int \mathcal{D}\phi \mathcal{D}\psi \exp \left\{ \int_0^\beta \int_0^L d\tau dx l_{tot}(\phi, \psi) \right\}. \quad (17)$$

Following standard prescription in field theory, let us consider the vacuum transition amplitude in the presence of sources $J(x)$'s. In this approach, the interactions can be represented by linear forms of the sources in term of the free particle lagrangian l_0 ,

$$Z_0[J_\psi(x), J_\phi(x)] = \int \mathcal{D}\phi \mathcal{D}\psi \exp \left\{ \int d^2x [l_0(\phi, \psi) + J_\phi(x)\phi(x) + J_\psi(x)\psi(x)] \right\}, \quad (18)$$

where $l_0(\phi, \psi) = \frac{1}{2}\partial_\mu\phi\partial^\mu\phi + \frac{1}{2}m_\phi^2\phi^2 + \frac{1}{2}\partial_\mu\psi\partial^\mu\psi$ and $\int d^2x = \int_0^\beta \int_0^L d\tau dx$. Thereafter, the desired interactions are derived by taking its derivatives up to certain power with respect to J 's at zero points.

For instance, the ψ^4 term in Eq. (3) can be derived through the 4th derivative of Z_0 in Eq. (eq:Z0) with respect to J_ψ at $J_{\phi,\psi} = 0$,

$$\left. \frac{\delta^4 Z_0}{\delta J_\psi^4(x)} \right|_{J_\phi=0, J_\psi=0} = Z_0 \psi^4(x). \quad (19)$$

One can perform the same procedure to obtain another interaction terms,

$$\left. \frac{\delta^4 Z_0}{\delta J_\phi^2 \delta J_\psi^2} \right|_{J_\phi=0, J_\psi=0} = Z_0 \phi^2 \psi^2, \quad (20)$$

and so forth. This means one can represent the interactions terms in term of differential functional operators which then simplify the complete generating functional to be,

$$Z = \exp \left\{ \int d^2x \left(-\frac{\lambda}{4} \frac{\delta^4}{\delta J_\psi^4} + \Lambda \frac{\delta^4}{\delta J_\phi^2 \delta J_\psi^2} \right) \Big|_{J_\phi=0, J_\psi=0} \right\} Z_0[J_\phi, J_\psi]. \quad (21)$$

4.1. Partition function

The integral in Eq. (17) can be evaluated analytically using the Gaussian integral. This can be accomplished by rewriting it in term of Gaussian integral using the Fourier representation of Green's function, that is [15],

$$(\partial_\mu\phi)(\partial^\mu\phi) = -\phi\Box\phi, \text{ and } (\partial_\mu\psi)(\partial^\mu\psi) = -\psi\Box\psi, \quad (22)$$

with the D'Alembertian stands for,

$$\square \equiv -\frac{\partial^2}{\partial t^2} - \frac{\partial^2}{\partial x^2}. \quad (23)$$

Substituting this result into Eq. (18) yields,

$$Z_0 = \int \mathcal{D}\phi \mathcal{D}\psi \exp \left\{ \int d^2x \left[-\frac{1}{2}\phi (\square + m_\phi^2) \phi - \frac{1}{2}\psi \square \psi + J_\phi \phi + J_\psi \psi \right] \right\} \quad (24)$$

Throughout the paper, for the sake of simplicity the fields are composed by its mean values corresponding to its classical trajectories and the quantum fluctuations around the mean value. Therefore, the fields can be expanded as [16],

$$\phi \equiv \bar{\phi}(x), \quad (25)$$

$$\psi \equiv \bar{\psi}(x) + \psi'(x), \quad (26)$$

where $\bar{\phi}$ and $\bar{\psi}$ are the mean fields of the classical path while ψ' is the dispersion of solutions. The variation of conformational field ϕ' is considered to be much less significant in the system. This is motivated by a fact that the protein is a classical matter with an infinitesimal dispersion relative to its mean value, *i.e.* its quantum aspect is negligible ($\phi' = 0$). The expression in Eq. (24) becomes,

$$Z_0 = \int \mathcal{D}\phi \mathcal{D}\psi \exp \left\{ - \int d^2x \left[\frac{1}{2}\bar{\phi}(\square + m_\phi^2)\bar{\phi} - J_\phi \bar{\phi} + \frac{1}{2}\bar{\psi} \square \bar{\psi} \right. \right. \\ \left. \left. + \frac{1}{2}\bar{\psi} \square \psi' + \frac{1}{2}\psi' \square \bar{\psi} + \frac{1}{2}\psi' \square \psi' - J_\psi \bar{\psi} - J_\psi \psi' \right] \right\}. \quad (27)$$

Using similar argument to obtain Eq. (22), one can apply the relation $\int \bar{\psi} \square \psi' d^2x = \int \psi' \square \bar{\psi} d^2x$ to get,

$$Z_0 = \int \mathcal{D}\phi \mathcal{D}\psi \exp \left\{ - \int d^2x \left(\frac{1}{2}\bar{\phi}(\square + m_\phi^2)\bar{\phi} - J_\phi \bar{\phi} + \frac{1}{2}\bar{\psi} \square \bar{\psi} \right. \right. \\ \left. \left. + \psi' \square \bar{\psi} + \frac{1}{2}\psi' \square \psi' - J_\psi \bar{\psi} - J_\psi \psi' \right) \right\}. \quad (28)$$

The classical path must satisfy the classical EOMs that are obtained from the lagrangian,

$$\square \bar{\psi}(x) = J_\psi(x) \quad \text{and} \quad (\square + m_\phi^2) \bar{\phi}(x) = J_\phi(x), \quad (29)$$

with the solutions,

$$\bar{\psi}(x) = \int \Delta_\psi(x-y) J_\psi(y) d^2y \quad \text{and} \quad \bar{\phi}(x) = \int \Delta_\phi(x-y) J_\phi(y) d^2y , \quad (30)$$

where $\Delta(x-y)$ is the Feynman propagator. Substituting Eqs. (29) and (30) into Eq. (28) yields,

$$\begin{aligned} Z_0 &= \exp \left\{ \frac{1}{2} \int d^2x d^2y [J_\phi(x) \Delta_\phi(x-y) J_\phi(y) + J_\psi(x) \Delta_\psi(x-y) J_\psi(y)] \right\} \\ &\times \int \mathcal{D}\psi' \exp \left\{ - \int d^2x \frac{1}{2} \psi' \square \psi' \right\} . \end{aligned} \quad (31)$$

Under this approximation, only ψ' remains in the path integral and the result is just a number, namely N .

Now the remaining task is calculating the transition amplitude by considering the Taylor expansion of Eq. (31),

$$\begin{aligned} Z_0 &= N \left\{ 1 + \frac{1}{2} \int d^2x d^2y [J_\phi(x) \Delta_\phi(x-y) J_\phi(y) + J_\psi(x) \Delta_\psi(x-y) J_\psi(y)] \right. \\ &+ \frac{1}{2!} \left(\frac{1}{2} \right)^2 \\ &\times \left(\int d^2x d^2y [J_\phi(x) \Delta_\phi(x-y) J_\phi(y) + J_\psi(x) \Delta_\psi(x-y) J_\psi(y)] \right)^2 \\ &\left. + \dots \right\} . \end{aligned} \quad (32)$$

Considering the higher order derivatives to retrieve the interaction terms as discussed before, the survived terms are,

$$\begin{aligned} Z_0 &\approx N \frac{1}{2!} \left(\frac{1}{2} \right)^2 \\ &\times \left(\int d^2x d^2y [J_\phi(x) \Delta_\phi(x-y) J_\phi(y) + J_\psi(x) \Delta_\psi(x-y) J_\psi(y)] \right)^2 \end{aligned} \quad (33)$$

This result is substituted into Eq. (21) to get,

$$Z = N e^\zeta \frac{\kappa^2}{8} , \quad (34)$$

where,

$$\zeta = \int d^2x \left(-\frac{\lambda}{4} \frac{\delta^4}{\delta J_\psi^4(x)} + \Lambda \frac{\delta^4}{\delta J_\phi^2(x) \delta J_\psi^2(x)} \right), \quad (35)$$

$$\kappa = \int d^2x_1 d^2x_2 [J_\phi(x_1) \Delta_\phi(x_1 - x_2) J_\phi(x_2) + J_\psi(x_1) \Delta_\psi(x_1 - x_2) J_\psi(x_2)] \quad (36)$$

$$+ \int d^2x_1 d^2x_2 [J_\phi(x_1) \Delta_\phi(x_1 - x_2) J_\psi(x_2) + J_\psi(x_1) \Delta_\psi(x_1 - x_2) J_\phi(x_2)] \quad (37)$$

With these notations, one can evaluate the survived term in $e^\zeta \kappa^2$,

$$\begin{aligned} \zeta \kappa^2 &= \int d^2x \left\{ -\frac{\lambda}{4} \frac{\delta^4 \kappa^2}{\delta J_\psi^4(x)} + \Lambda \frac{\delta^4 \kappa^2}{\delta J_\phi^2(x) \delta J_\psi^2(x)} \right\} \\ &= \int d^2x \{-6\lambda \Delta_\psi^2(0) + 8\Lambda \Delta_\phi(0) \Delta_\psi(0)\}. \end{aligned} \quad (38)$$

since,

$$\dot{\kappa}_\psi = \frac{\delta \kappa}{\delta J_\psi(x)} = \int d^2x_2 \Delta_\psi(x - x_2) J_\psi(x_2) + \int d^4x_1 J_\psi(x_1) \Delta_\psi(x_1 - x) \quad (39)$$

$$\dot{\kappa}_\phi = \frac{\delta \kappa}{\delta J_\phi(x)} = \int d^2x_2 \Delta_\phi(x - x_2) J_\phi(x_2) + \int d^2x_1 J_\phi(x_1) \Delta_\phi(x_1 - x) \quad (40)$$

$$\ddot{\kappa}_\psi = \frac{\delta^2 \kappa}{\delta J_\psi^2(x)} = 2\Delta_\psi(0), \quad (41)$$

$$\ddot{\kappa}_\phi = \frac{\delta^2 \kappa}{\delta J_\phi^2(x)} = 2\Delta_\phi(0). \quad (42)$$

Finally, this leads to,

$$Z = N \exp \left\{ \int_0^\beta d\tau \int_0^L dx \left[-\frac{3}{4} \lambda \Delta_\psi^2(0) + \Lambda \Delta_\phi(0) \Delta_\psi(0) \right] \right\}. \quad (43)$$

This is the master equation to investigate the statistical properties in the next subsection.

4.2. Statistical observables

Let us consider the specific heat of the system in a constant volume, C_V , that is a particular interest from experimental point of view. The specific heat can be derived directly from the partition function using the relation,

$$C_V = \beta^2 \left(\frac{\partial^2 \ln Z}{\partial \beta^2} \right)_V. \quad (44)$$

In the present case, it is found to be,

$$C_V = \beta^2 \frac{\partial^2}{\partial \beta^2} \left(\ln N - \beta L \left[\frac{3}{4} \lambda \Delta_\psi^2(0) - \Lambda \Delta_\phi(0) \Delta_\psi(0) \right] \right), \quad (45)$$

after performing the integration over τ and x respectively, while the overall factor N has been obtained as [13],

$$N = \frac{1}{4\pi \sinh(k\beta/2)}. \quad (46)$$

Next, one must find out the form of $\Delta(0)$. This can be achieved by solving the the Green function. Since the Feynman propagator $\Delta(x)$ obeys,

$$\begin{aligned} \left(-\frac{\partial^2}{\partial \tau^2} - \frac{\partial^2}{\partial x^2} \right) \Delta_\psi(x, \tau) &= \delta(x)\delta(\tau), \\ \left(-\frac{\partial^2}{\partial \tau^2} - \frac{\partial^2}{\partial x^2} + m_\phi^2 \right) \Delta_\phi(x, \tau) &= \delta(x)\delta(\tau), \end{aligned} \quad (47)$$

and taking a particular form of Green functions [17],

$$\begin{aligned} \Delta_\psi(x, \tau) &= \int \frac{dk}{2\pi} e^{ikx} \Delta_\psi(\tau), \\ \Delta_\phi(x, \tau) &= \int \frac{dq}{2\pi} e^{iqx} \Delta_\phi(\tau), \end{aligned} \quad (48)$$

the imaginary-time propagators $\Delta(\tau)$ should satisfy the following differential equations,

$$\begin{aligned} \left(-\frac{\partial^2}{\partial \tau^2} + k^2 \right) \Delta_\psi(\tau) &= \delta(\tau), \\ \left(-\frac{\partial^2}{\partial \tau^2} + q^2 + m_\phi^2 \right) \Delta_\phi(\tau) &= \delta(\tau). \end{aligned} \quad (49)$$

Imposing the Dirichlet periodic boundary conditions,

$$\Delta\left(-\frac{\beta}{2}\right) = \Delta\left(\frac{\beta}{2}\right) \text{ and } \dot{\Delta}\left(-\frac{\beta}{2}\right) = \dot{\Delta}\left(\frac{\beta}{2}\right), \quad (50)$$

and using Eq. (49), Eq. (48) becomes [18],

$$\Delta_\psi(\tau) = \frac{\cosh(k(\beta/2 - |\tau|))}{2k \sinh(k\beta/2)}, \quad (51)$$

$$\Delta_\phi(\tau) = \frac{\cosh\left(\sqrt{q^2 + m^2}(\beta/2 - |\tau|)\right)}{2\sqrt{q^2 + m^2} \sinh\left(\beta\sqrt{q^2 + m^2}/2\right)}. \quad (52)$$

Therefore the Fourier representation of Green functions can be written as

$$\Delta_\psi(x, \tau) = \int \frac{dk}{2\pi} \frac{e^{ikx} \cosh(k(\beta/2 - |\tau|))}{2k \sinh(k\beta/2)}, \quad (53)$$

$$\Delta_\phi(x, \tau) = \int \frac{dq}{2\pi} \frac{e^{iqx} \cosh(\sqrt{q^2 + m^2}(\beta/2 - |\tau|))}{2\sqrt{q^2 + m^2} \sinh(\beta\sqrt{q^2 + m^2}/2)}. \quad (54)$$

As can be seen, the propagator $\Delta_\phi(x, \tau)$ in Eq. (54) contains a factor of $\sqrt{q^2 + m_\phi^2}$ which makes the integral cannot be performed analytically. In this paper, it is done numerically.

Performing the integrals in Eqs. (53) and (54), and substituting the results into Eq. (45), one then obtains the numerical results as shown in Figs. 2 and 3 for various values of λ and Λ , while $k = 0.01$. The values of another variables are the same as in Fig. 1.

5. Conclusion

An extension of the phenomenological model describing the conformational dynamics of proteins has been briefly reintroduced. The model based on the matter interactions among the conformational field and the nonlinear sources represented as the scalar bosonic fields ϕ and ψ . As already shown in our previous work [3], the nonlinear and tension force terms appear naturally from the scalar lagrangian with ψ^4 self-interaction. Moreover, such forces are realized as a consequence of symmetry breaking.

In the present paper, the numerical simulation of protein folding dynamics has been refined to revise some technical errors in the previously reported result [3]. However, the figure has only changed slightly, while the conclusion remains the same.

Moreover, in the present paper the statistical properties of protein folding within the model are studied in detail. In particular, the specific heat, C_V , has been calculated analytically using statistical mechanics and path integral method. The evolution of C_V in term of temperature has been shown for various levels of nonlinearity and interaction with nonlinear source represented by λ and Λ . It is found that both of them contribute in an opposite way, and could completely cancel each other at certain values as Eq. (6) is fulfilled. This occurs when the symmetry is maximally broken. This also means that

increasing energy absorption prefers high level of nonlinearity of sources and at the same time weak interaction between the sources and protein backbone.

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References

- [1] C. M. Dobson, Protein folding and misfolding, *Nature* 426 (2003) 884.
- [2] S. F. Mingaleev, Y. B. Gaididei, P. L. Christiansen, Y. Kivshar, Nonlinearity-induced conformational instability and dynamics of biopolymers, *Europhysics Letter* 59 (2002) 403. doi:[10.1209/eppl/i2002-00209-3](https://doi.org/10.1209/epl/i2002-00209-3).
- [3] M. Januar, A. Sulaiman, L. T. Handoko, Conformational changes and protein folding induced by ϕ^4 interaction, in: Proceeding of the Conference in Honour of Murray Gell-Mann's 80th Birthday : Quantum Mechanics, Elementary Particles, Quantum Cosmology and Complexity, World Scientific, 2011, pp. 472–479. doi:[10.1142/9789814335614_0047](https://doi.org/10.1142/9789814335614_0047).
- [4] S. Caspi, E. Ben-Jacob, Toy model studies of soliton-mediated protein folding and conformation changes, *Europhysics Letter* 47 (1999) 522. doi:[10.1209/eppl/i1999-00419-1](https://doi.org/10.1209/eppl/i1999-00419-1).
- [5] N. G. Berloff, Nonlinear dynamics of secondary protein folding, *Physics Letter A* 337 (2005) 391. doi:[10.1016/j.physleta.2005.01.080](https://doi.org/10.1016/j.physleta.2005.01.080).
- [6] S. Caspi, E. Ben-Jacob, Conformation changes and folding of proteins mediated by Davydov's soliton, *Physics Letter A* 272 (2000) 124. doi:[10.1016/S0375-9601\(00\)00413-8](https://doi.org/10.1016/S0375-9601(00)00413-8).
- [7] A. Garcia, J. Onuchi, Folding a protein in a computer: an atomic description of the folding/unfolding of protein a, *Proceedings of the National Academy of Sciences of the United States of America* 100 (2003) 13898.

- [8] J. N. Onuchi, P. G. Wolynes, Theory of protein folding, *Current Opinion in Structural Biology* 14 (2004) 70. doi:10.1016/j.sbi.2004.01.009.
- [9] A. Sulaiman, L. T. Handoko, The effects of bio-fluid on the internal motion of DNA, *Journal of Computational and Theoretical Nanoscience* 8 (2011) 124–132, arXiv:1012.2444. doi:10.1166/jctn.2011.1669.
- [10] A. Sulaiman, F. P. Zen, H. Alatas, L. T. Handoko, Anharmonic oscillation effect on the Davydov-Scott monomer in thermal bath, *Physical Review E* 81 (2010) 061907, arXiv:1002.0069. doi:10.1103/PhysRevE.81.061907.
- [11] A. Sulaiman, F. P. Zen, H. Alatas, L. T. Handoko, Statistical mechanics of Davydov-Scott's protein model in thermal bath, in: Proceeding of the Conference in Honour of Murray Gell-Mann's 80th Birthday : Quantum Mechanics, Elementary Particles, Quantum Cosmology and Complexity, World Scientific, 2011, pp. 661–668, arXiv:1103.1677. doi:10.1142/9789814335614_0072.
- [12] J. H. Mathews, K. D. Fink, Numerical Methods using Matlab 4th Ed., Prentice-Hall, 2004.
- [13] R. MacKenzie, Path integral methods and applications, in: Lecture notes in 6th Vietnam School of Physics, 2000, p. 28.
- [14] J. I. Kapusta, C. Gale, Finite-Temperature Field Theory: Principles and Applications 2nd Ed., Cambridge University Press, 2006.
- [15] L. H. Ryder, Quantum Field Theory 2nd Ed., Cambridge University Press, 1996.
- [16] R. P. Feynman, A. R. Hibbs, Quantum Mechanics and Path Integrals, McGraw-Hill, 1965.
- [17] M. L. Bellac, Thermal Field Theory, Cambridge University Press, 1996.
- [18] R. Rattazzi, The Path Integral Approach to Quantum Mechanics, EPFL, 2009.

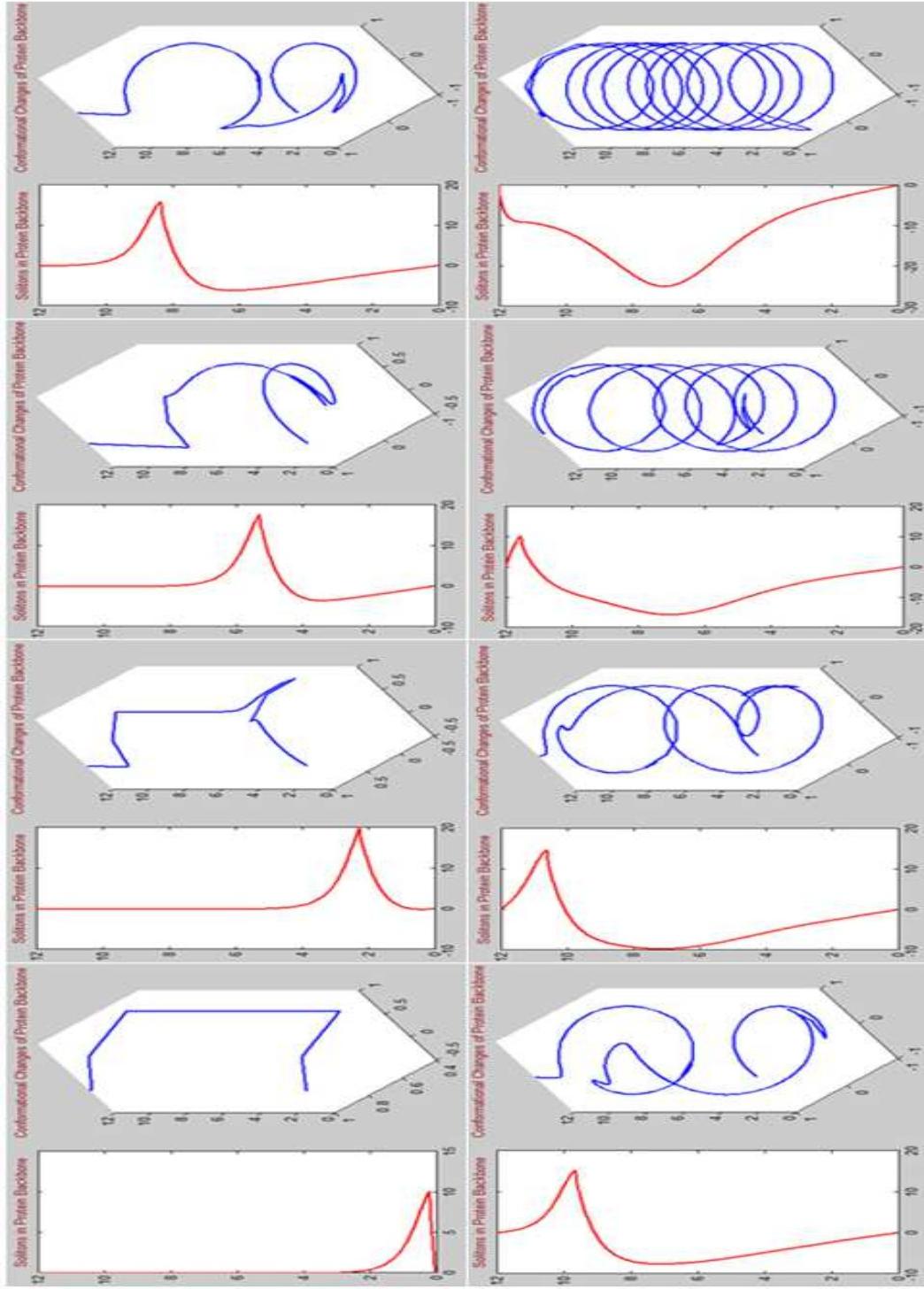


Figure 1: The soliton propagations and conformational changes on the protein backbone inducing protein folding. The vertical axis in soliton evolution denotes time in second, while the horizontal axis denotes its amplitude. The conformational changes are on the (x, y, z) plane.

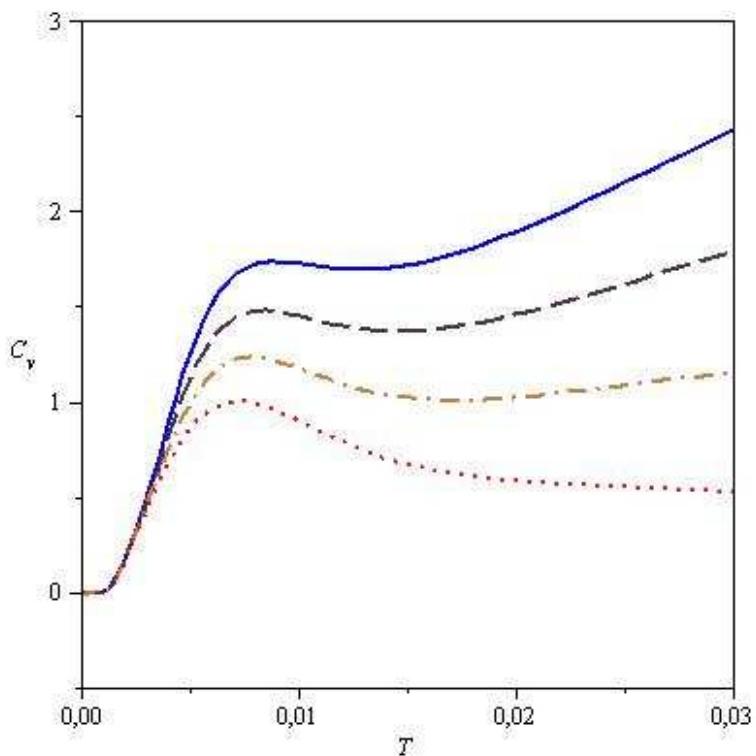


Figure 2: C_V as a function of temperature for various values of $\lambda = 0.0003$ (solid-line), 0.0012 (dashed-line), 0.0021 (dashed-dotted-line), 0.0030 (dotted-line) with $\Lambda = 0.00283$.

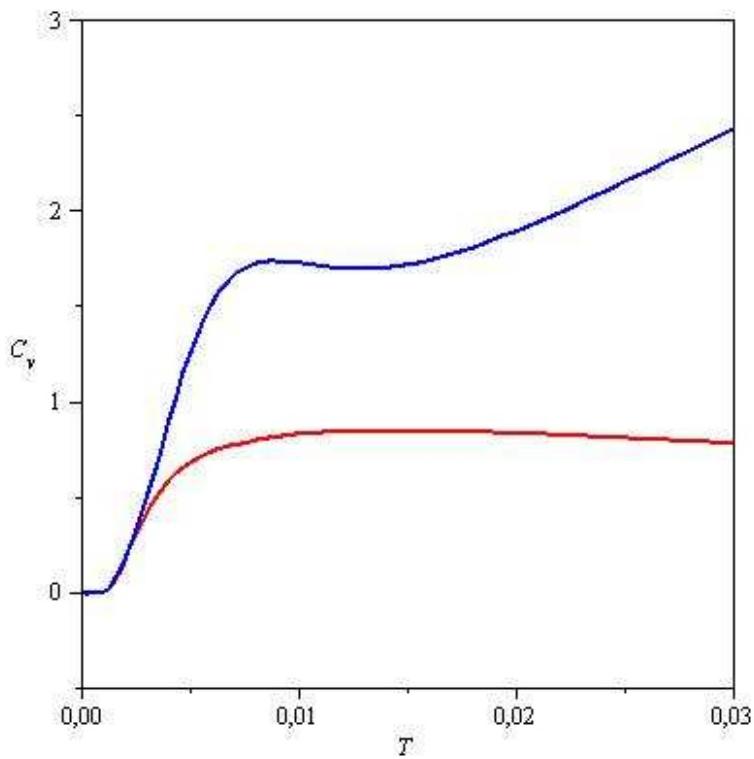


Figure 3: C_V as a function of temperature for $\Lambda = 0.00283$ (blue-line) and 0 (red line) with $\lambda = 0.0003$.